DAIDS Requirements for US Laboratories
Guidance to Investigators Applying for Funding to Conduct HIV/AIDS Clinical Trials

1.0 Diagnosis, Safety tests, CD4 and Virological tests, and Primary endpoints

Tests that are used for diagnosis of infection (e.g., HIV, CMV, HSV, Syphilis), determining eligibility (e.g., pregnancy test), monitoring the safety of the intervention (e.g., hematology, chemistry), making patient management decisions (e.g., CD4, viral load), or as primary study endpoints, must be performed in laboratories that are CLIA certified/accredited (http://www.cms.hhs.gov/clia/), or equivalent. Tests must be quality assured by external proficiency testing surveys provided by the College of American Pathologists (CAP) or equivalent, and the use of FDA-approved methodologies is strongly encouraged. If non-approved methods are considered, these must be validated in a study that compares a proposed method to an FDA-approved one. Guidelines for conducting a validation study are described in the Method Validation document:
http://www3.niaid.nih.gov/research/resources/DAIDSClinRsrch/PDF/labs/MethodValidation.pdf

Laboratories should be conducting operations in a Good Clinical Laboratory Practices (GCLP) manner. The elements of GCLP are described in the attached document:
http://www3.niaid.nih.gov/NR/rdonlyres/6837341A-D644-4D40-A0F0-E66995201B45/0/ElementsOfGCLP.doc

A. CD4 testing

CD4 determinations must be done according to CDC guidelines that describe dual-platform technology - MMWR 1997;46 [No. RR-2, http://www.cdc.gov/mmwr/preview/mmwrhtml/00045580.htm or single-platform technology - MMWR 2003;52(RR-2), http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5202a1.htm.

If CD4 is a primary endpoint of the proposed trial, the laboratory that performs CD4 testing must participate in the DAIDS Immunology Quality Assessment (IQA) CD4 proficiency testing (PT) program. More information about this program may be found at: http://aactg.s-3.com/iqa.htm.

To request enrollment in this program, please contact Daniella Livnat at 301 435 3775 or email to dlivnat@niaid.nih.gov. Upon enrollment in the IQA CD4 PT program, laboratories are considered 'Provisionally Certified'.

There is no fee for participating in this program.

B. Virological tests

The use of FDA-approved methods is strongly encouraged.

Consensus virological methods can be found at: http://aactg.s-3.com/labmanual.htm

If HIV RNA PCR or HIV DNA PCR or genotypic resistance testing is a primary endpoint of the proposed trial, laboratories that perform these tests must participate in the DAIDS Virology Quality Assurance (VQA) program that provides proficiency testing panels for each of these tests. Also, if HIV DNA PCR or genotypic resistance testing is to be used for diagnosis and/or to make decisions about subject management as part of the proposed trial, these tests must be monitored by proficiency testing provided by the VQA. More information about this program may be found at: http://aactg.s-3.com/vqa.htm.

To request enrollment in VQA PT programs, please contact Joe Fitzgibbon at 301 451 2738 or email to jfitzgibbon@niaid.nih.gov. For HIV viral load, VQA certification requires acceptable test results of an initial panel of 20 coded samples and two subsequent five-sample panels. The process of achieving certification takes at least five months.

There is no fee for participating in this program.

For requirements described in Section I above, please include the following in the Comprehensive Laboratory Plan:

- A spreadsheet that lists all the tests that will be done for the study, all the laboratories in which these tests will be done, and the external QA providers and proficiency testing surveys that will be used to monitor each test. The template below is provided for your convenience as an example of how this information can be provided. You may modify this as appropriate:

  http://www3.niaid.nih.gov/NR/rdonlyres/C1076997-2029-42B5-AC25-39E53E8C4686/0/LabSpreadsheet.xls

- Complete identifying information for all the laboratories that will participate in the study

- Proof of CLIA (or equivalent) certification for each laboratory

DAIDS will verify participation and successful performance of the laboratory in the various proficiency testing programs.

2.0 Research Use Only (RUO) endpoint tests (research tests not yet validated and approved by an ICH regulatory body such as the FDA)

Research Use Only endpoint tests (e.g., ELISPOT, ICC, pharmacological, virological) should be performed in laboratories that conduct operations in a Good Clinical Laboratory Practices (GCLP) manner. External proficiency testing should be applied to such tests. If existing proficiency testing surveys are not available, a suitable form of alternative proficiency assessments needs to be devised and proposed.

A description of the elements of GCLP and a comprehensive presentation about GCLP are found above under I. The training of laboratory staff in the principles of GCLP is strongly encouraged. For information about DAIDS-sponsored GCLP training workshops, please contact Janice Darden at jdarden@niaid.nih.gov.

For requirements described in Section II above, please include the following in the Comprehensive Laboratory Plan:

- A list of the RUO tests
- Test standard operating procedures in a format that includes information about test principle, specimen requirements, reagents, supplies and equipment, procedure, calculations, quality control, procedural notes and references
- Complete identifying information for the laboratories indicated above
- A description of the external proficiency testing measures undertaken for each test in each laboratory
- A documentation of the ability of staff to proficiently perform proposed tests
- A description of the GCLP operations in the laboratory

3.0 Study specimen management plan

Each study must have a specimen management plan that describes sample acquisition, recording, testing, storing and shipping, including specimen flow chart, QA oversight and corrective action (the latter two may be included in the Laboratory QA plan). If shipments of specimens are to occur, they must be done according to the most current International Air Transport Association (IATA) shipping regulations: http://www.iata.org/ps/publications/9065.htm.

For requirements described in Section III above, please include the following in the Comprehensive Laboratory Plan:

- The specimen management plan
- Proof of training in IATA shipping regulations (certification) if specimen shipments are planned for the study

4.0 Study laboratory Data Management plan

Each study must include a laboratory data management plan that describes the systems and processes for acquisition, recording, data entry, exporting, reporting, modification, security, and archiving of laboratory test results. The plan should describe the QA oversight and corrective actions, and how all laboratory test results will be integrated into the general study database. If the laboratory plans to use a Laboratory Information Management System (LIMS) or a Laboratory Data Management System (LDMS), these should be 21 CFR part 11 compliant: http://www.fda.gov/ora/compliance_ref/part11/.

For requirements described in Section IV above, please include the following in the Comprehensive Laboratory Plan

- The laboratory data management plan
- A description of the testing that was done to ensure that data flow smoothly and maintain integrity from the point of acquisition to the study database
- Proof of 21 CFR part 11 compliance if available

5.0 Laboratory QA plan (for non-CLIA laboratories)

The study must have a laboratory quality assurance plan to regularly review all components of laboratory activities, including intervention and corrective action plan, and plans for backup testing facilities. See the Elements of QA Plan described in the attached document: http://www3.niaid.nih.gov/NR/rdonlyres/6AFF42D5-58BB-4A79-BF52-78AE156FEB2C/0/ElementsOfQMPlan.doc

For requirements described in Section V above, please include the following in the Comprehensive Laboratory Plan:

- The laboratory QA plan

6.0 Laboratory-specific auditing (of non-CLIA endpoint laboratories) - provided by DAIDS

DAIDS and/or its contractors will conduct laboratory-specific audit visits to determine laboratory readiness to participate in trials, and, as indicated, during the conduct of a trial. The DAIDS laboratory assessment document defines the scope of the DAIDS Lab Audit: http://www3.niaid.nih.gov/NR/rdonlyres/C012BE9C-88EC-476A-89D5-4338ED612748/0/DAIDSLabAudit.doc